Right to care

TREATING AIDS SERIOUSLY

TB and HIV
Treatment of Co-infection

Dr Ian Sanne

SOUTH AFRICA AND THE UNITED STATES

WORKING IN PARTNERSHIP

USAID FROM THE AMERICAN PEOPLE

- *Tuberculosis is the most important coinfection in the HIV epidemic.*
- *In sub-Saharan Africa, it is estimated that 50% of HIV-1-infected patients will develop TB in their lifetime, and there is a 10% annual risk of developing TB.*

- SA Guidelines
- Development of TB before HAART
  - **CD4+ > 200 cells/mm^3** and not WHO Stage 4
    - reassess for HAART after completing TB Rx
  - **CD4+ < 200 cells/mm^3** or WHO Stage 4
    - complete 2 mo TB Rx before starting HAART
  - **CD4+ < 50 cells/mm^3** or other serious HIV-related illness
    - complete at least 2 weeks' TB Rx before initiating HAART (regimen 1a)

SA national ART guidelines, 2004

SA GUIDELINES

- Development of TB on HAART
  - continue HAART
  - If on NVP, change to EFZ (or continue NVP with monthly ALT monitoring)
  - If on Regimen 2, increase Lopinavir/Ritonavir to 400/400 mg 12 hrly, or Saquinavir/Ritonavir

SA national ART guidelines, 2004

2 important questions

- “When to start ARV’s in patients presenting with Active TB?”

- Composition of ARV regimen and TB treatment and duration of treatment

Interactions between TB and HIV Rx

- Paradoxical worsening of TB with the introduction of ARV's
- Drug Interactions
- Overlapping Drug Toxicities
- Treatment adherence – pill burden, symptoms related to drug toxicities

2 important questions

- "When to start ARV's in patients presenting with Active TB?"

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WHO Guideline and SA Guideline

- Initiate TB treatment and delay ART for first 2 months or the intensive phase of treatment

- However mortality rates in HIV-1-infected patients with TB in the absence of ART are extraordinarily high.
- Early initiation of therapy could improve outcomes by reducing TB-related mortality and HIV-related mortality.
- Early initiation of ART could also reduce HIV-associated morbidity, particularly among individuals with very low CD4 cell counts.

Potential problems associated with treating both HIV and TB

- Pill burden and symptoms related to treatment
- Overlapping toxicities of ART and TB treatment
- Immune reconstitution and paradoxical worsening of TB
- Risk that one treatment might disrupt management of the other

SIDE-EFFECTS: ART AND TB Rx

	Antiretroviral Rx	TB Rx
nausea	**ddI, AZT, RTV, SQV**	**PZA**
hepatitis	**NVP, EFZ**	**Rif, INH, PZA**
peripheral neuropathy	**d4T, ddI**	**INH**
rash	**NVP, EFZ**	**Rif, INH, PZA**

Recent drug toxicity data

- SQV/RTV and Rifampicin should not be used together as these drugs cause hepatotoxicity, potentially fatal
- This is likely to be related to RTV and further warnings for the use of Kaletra with additional RTV will follow
- Additional drugs need to be explored for combination treatment in second line treatment

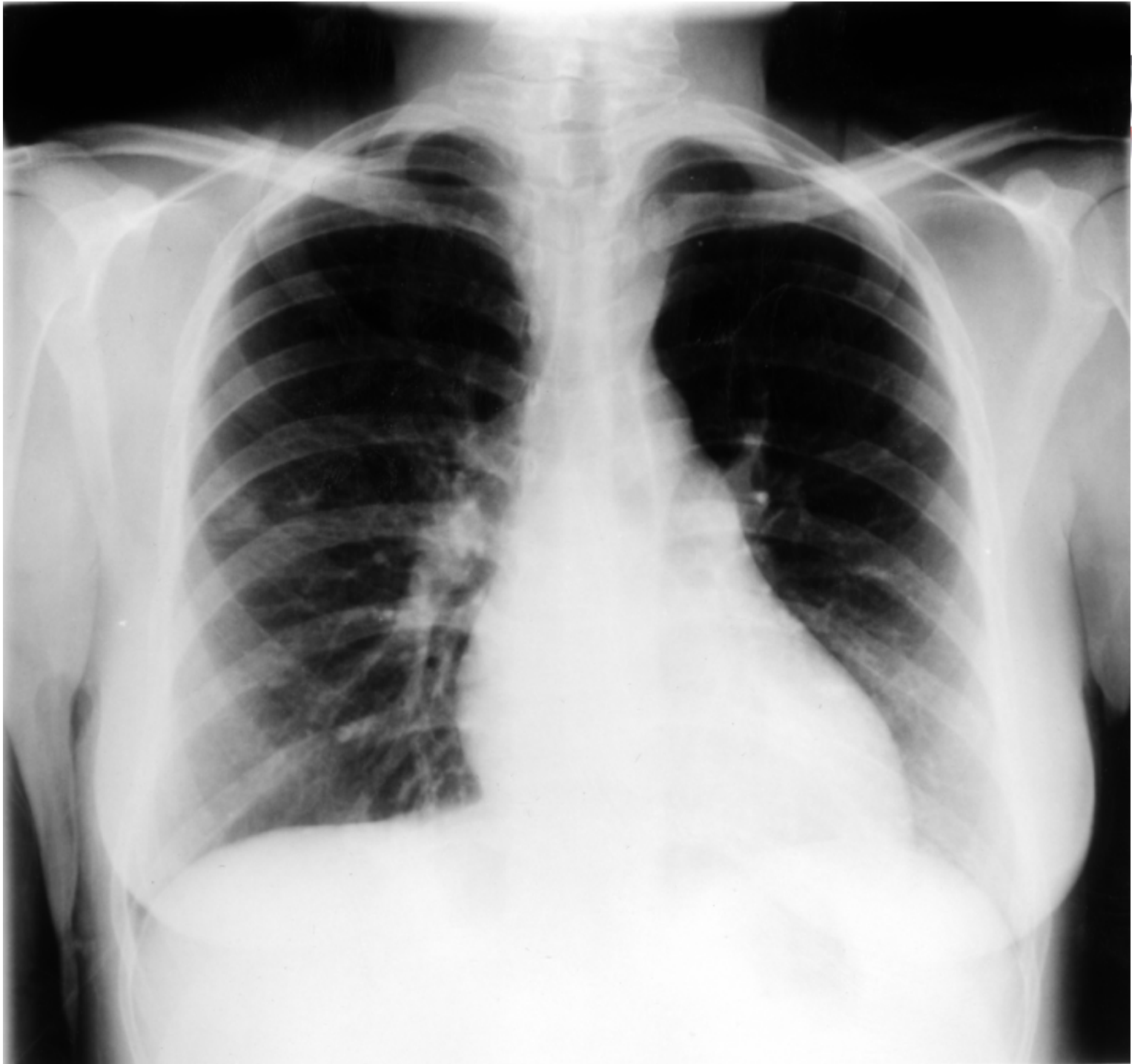
Immune Reconstitution and Paradoxical TB responses

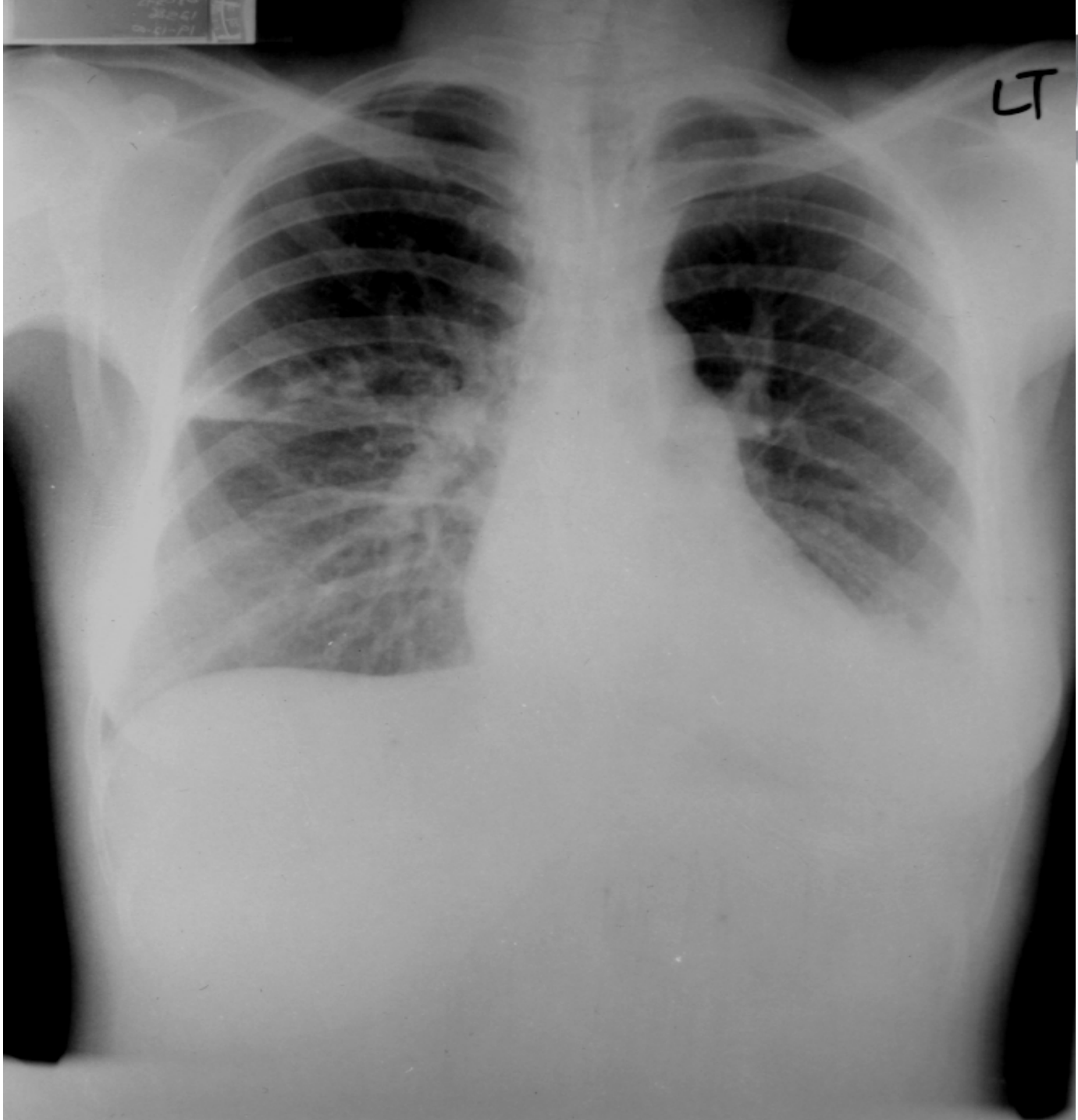
- Given as a reason to delay antiretroviral therapy
- Uncertain whether a delay in treatment by 2 months will prevent this predominantly immune mediated disease manifestation
- No definitive data on the incidence in patients stratified by their baseline CD4+ count and by the TB disease presentation

IMMUNE RECONSTITUTION SYNDROME (PARADOXICAL RESPONSE)

- Deterioration of the TB disease after the initiations of the TB treatment
- ART and associated immune reconstitution may lead to an unmasking of undiagnosed TB and or worsening active TB
- Differential diagnosis include non-adherence, inadequate treatment, drug resistance (MDR TB), and other co-morbid diseases
- Treatment should include continued ART, addition of oral steroid therapy and testing for TB drug resistance.

- Manifestations of immune reconstitution syndrome
  - Fever, marked improvements in CD4+ count
  - new or enlarging lymph nodes
  - new or worsening pulmonary infiltrates
  - new or increasing pleural effusion, pericardial effusion or ascites
  - new or worsening meningitis, intracranial tuberculomas
  - disseminated skin lesions
  - epididymitis
  - hepatosplenomegaly
  - soft tissue abscesses

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Effect of Rifampin on serum concentrations of Protease Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors

PI		NNRTI	
Saquinavir	↓ 80%	Nevirapine	↓ 37-58%
Ritonavir	↓ 35%	Efavirenz	↓ 13-26%
Indinavir	↓ 90%		
Nelfinavir	↓ 82%		
Amprenavir	↓ 81%		
Lopinavir/ritonavir	↓ 75%		
Atazanavir	not done		

David Cohn
3rd Global TB/HIV Working Group meeting
Montreux, Switzerland
June 2003

References

- AIDS Bulletin

Juggling Act: How Do We Combine TB and HIV Therapy?

Jay F. Dobkin, MD

- AIDS
  Implementing Antiretroviral Therapy in Resource-Constrained Settings: Opportunities and Challenges in Integrating HIV and Tuberculosis Care

Salim S. Abdool Karim et al

- A5221 AACTG protocol